REMARKS

Claims 1-6, 11-12, 14-19, 23-40, 48, 49, and 52-55 were pending in this application. Claims 2-6, 35, 36, and 38-40 were withdrawn by the Examiner. Claims 2-6 and 40 are now canceled without prejudice as drawn to non-elected Groups. Claims 11, 12, 14-18, 34 and 55 are also canceled. Applicants reserve the right to pursue the canceled subject matter in a related application.

Claims 1, 19, 25, 33, 37, and 52 are amended herein. Support for the amendment of claims 1, 19, and 25 can be found throughout the specification, for example at page 16, line 24 through page 18, line 2, and in original claims 4 and 12. Support for the amendment of claim 33 can be found in original claim 33. Support for the amendment of claim 37 can be found in the specification at page 7, line 1 and at page 28, line 30 through page 30, line 20. Support for the amendment of claim 52 can be found in the specification at page 28, lines 8-28.

The specification, at page 14, lines 9, 17-18, and 33, has been amended to remove hyperlinks and other forms of browser-executable code. The specification at page 19, lines 20 and 35, has been amended to correct the format of a reference to a trademark.

No new matter is introduced by these amendments. Unless specifically stated otherwise, none of these amendments is intended to limit the scope of any claim.

After entry of this amendment **claims 1, 19, 23-33, 35-39, 48-49 and 52-54 are pending**, of which claims 35, 36, 38, and 39 are currently withdrawn from consideration in this application. Consideration and allowance of the pending claims is requested.

Formalities from Office Action:

Applicants acknowledge that the election of Group II (claims 1, 10-12, 26-32, 48-49, and 52-55), Group III (claims 1, 13-18, 25-32, 48-49, and 52-55) and claims 19, 23, and 24 is made final. Applicants note the Examiner's statement "if claims reciting a given fusion protein are found to be free of the art of record, the corresponding nucleic acid claims will be rejoined"

(Office action at page 3, line 9). Thus, claims 35, 36, 38 and 39, directed to nucleic acids, are withdrawn but maintained in the application.

Claim Objections:

Claim 14 was objected to for being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 16 was objected to because the claim recites nomenclature that is inconsistent with the specification. Claims 14 and 16 have been canceled, rendering these objections moot.

Amendments to the Specification:

The specification was objected to because the trademark QIAexpress™ was not capitalized. The specification has been amended at page 19, lines 20 and 35, to recite QIAEXPRESS™. The generic terminology of the trademark (expression system) accompanies the trademark at page 19, lines 20 and 35.

The specification was also objected to because it contained embedded hyperlinks and other forms of browser-executable code. The specification has been amended at page 14, lines 9, 17-18, and 33 to remove the hyperlink and other forms of browser-executable code.

Applicants respectfully request that the objections to the specification be withdrawn.

Claim Rejections Under 35 U.S.C. §112, first paragraph:

Claims 16, 18, 33-34 and 37 (written description)

Claims 16, 18, 33-34 and 37 have been rejected under 35 U.S.C. §112, first paragraph because the claims allegedly contain subject matter that was not described in the specification in such a way as to enable one of skill in the art to make or use the invention. Applicants respectfully traverse this rejection.

Applicants have canceled claims 16, 18, and 34, rendering the rejection of these claims moot.

Claims 33 and 37 are rejected on the ground that a public deposit of the molecule recited in the claims is required for the enablement of this claim. Applicants respectfully traverse this rejection. MPEP §2402 states that a deposit may be required if "words alone cannot sufficiently describe how to make and use the invention." Furthermore, 37 C.F.R. §1.802(b) states that "[b]iological material need not be deposited, inter alia, if it is known and readily available to the public or can be made or isolated without undue experimentation."

Claim 37 has been amended to depend from claim 1 and recites "The protein of claim 1, wherein the protein is encoded by a nucleic acid molecule having a sequence as set forth in SEQ ID NO: 4," wherein SEQ ID NO: 4 sets forth the nucleic acid sequence encoding sCD4-SCFv(17b). Similarly, the amino acid sequence of sCD4-SCFv(17b) is provided in SEQ ID NO: 3. The provided amino acid and nucleic acid sequences of sCD4-SCFv(17b) clearly describe and enable the invention, and the specification provides additional support for making and using it. For instance, the specification at page 28, lines 32-33 describes that sCD4 is the C-terminus 183 amino acids of CD4 and the specification at page 28, line 31 through page 30, line 20, describes the generation of the sCD4-SCFv(17b) nucleic acid fusion construct. Thus, sCD4-SCFv(17b) is clearly enabled by the specification and the sequence listing, and a deposit is not required. Applicants respectfully request that the rejection of amended claims 33 and 37 be withdrawn.

Claims 1, 11-12, 14-19, 23-32, 48-49, and 52-55 (enablement)

Claims 1, 11-12, 14-19, 23-32, 48-49, and 52-55 have been rejected under 35 U.S.C. §112, first paragraph for allegedly not being enabled for "a neutralizing bispecific fusion protein capable of binding to an inducing site on gp120 (CD4 binding site) thereby exposing an induced epitope of gp120 (co-receptor binding site) and a second binding domain capable of forming a neutralizing complex with the induced epitope wherein the first binding domain is anything other than sCD4 and the second binding domain is anything other than SCFv(12b[17b])." Applicants traverse this rejection.

The Office action repeatedly refers to the second binding domain as SCFv(12b) (see, for example, page 6, lines 6 and 11). Applicants believe that "12b" is intended to be "17b," and will respond to the rejection based on this belief.

Claims 11, 12, 14-18, and 55 have been canceled, rendering the rejection of these claims moot.

Applicants respectfully but strenuously traverse the rejection of the remaining claims, and reserve the right to contest this rejection in a later application. Solely in the interest of advancing prosecution in the current application, Applicants have amended claim 1 to recite that the "first binding domain is sCD4 and the second binding domain is SCRv(17b)." Claims 19, 23-32, 48-49, and 52-54 depend, either directly or indirectly, from claim 1 and thereby incorporate the amendment.

The current Office action, at page 6, lines 1-6, confirms that there is enablement for "a neutralizing bispecific fusion protein capable of binding to an inducing site on gp120 (CD4 binding site) thereby exposing an induced epitope of gp120 (co-receptor binding site) and a second binding domain capable of forming a neutralizing complex with the induced epitope wherein the first binding domain is sCD4 and the second binding domain is SCFv(12b[17b])." Since the Office action acknowledges that the amended claim scope is enabled, Applicants respectfully request that this rejection of claim 1, and all claims depending therefrom, be withdrawn.

Claims 49 and 55 (enablement)

Claims 49 and 55 are further rejected on the ground that pharmaceutical compositions (claim 49) and kits containing the pharmaceutical compositions (claim 55) are not enabled by the specification. Applicants traverse this rejection.

Claim 55 has been canceled, rendering the rejection of this claim moot.

Regarding claim 49, there is ample enablement for the claimed pharmaceutical composition. For instance, Section V, beginning on page 25, describes making pharmaceutical compositions that comprise a bispecific fusion protein. In addition, ample teaching is provided on how to use such compositions. The specification at page 26, line 9 through page 28, line 6 describes the clinical use of bispecific fusion proteins. Particularly, page 27, lines 6-10, states that the sCD4-SCFv(17b) fusion protein is useful in the prevention of infection during or immediately after HIV exposure and indicates that the bispecific fusion protein can be administered before or soon after the HIV exposure. In addition, the specification at page 32, line 7 through page 33, line 26 describes methods demonstrating that sCD4-SCFv(17b) strongly inhibits HIV-1 Env-mediated cell fusion. Thus, the specification clearly teaches how a pharmaceutical composition comprising an sCD4-SCFv(17b) bispecific fusion protein can be used and that it is effective in a cellular system.

MPEP §2164.02 states that "[c]ompliance with the enablement requirement of 35 U.S.C. §112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic." . . . An applicant need not have actually reduced the invention to practice prior to filing." The specification at page 34, lines 11-26 includes prophetic examples of the *in vivo* use of the sCD4-SCFv(17b) bispecific fusion protein.

The specification is enabling for making and using a pharmaceutical composition as claimed in claim 49. Applicants respectfully request that the rejection of claim 49 be withdrawn.

Claim Rejections Under 35 U.S.C. §112, second paragraph:

Claims 33, 34, and 37 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants traverse this rejection.

Claim 34 has been canceled, thereby rendering the rejection of this claim moot. Claim 33 has been amended to remove the term "functional." Claim 37 is no longer dependent on a non-elected invention, as it has been amended to be dependent from claim 1. Applicants therefore respectfully request that the rejection of claims 33 and 37 be withdrawn.

Claim Rejections Under 35 U.S.C. §103(a):

Traunecker et al. *in view of Sullivan* et al.

Claims 1, 11-12, 14-19, 23-34, 37, 48-49, and 52-55 are rejected as allegedly rendered obvious by Traunecker *et al.* (*International Journal of Cancer*, Supplement 7, 51-52, 1992) in light of Sullivan *et al.* (*Journal of Virology*, 72(6):4694-4703, 1998). Applicants traverse this rejection, as these documents, even in combination, do not teach or fairly suggest all of the elements of the claimed invention.

Applicants have canceled claims 11, 12, 14-18, 34 and 55 rendering the rejection of these claims moot. As described above, Applicants have amended claim 1 to recite that the "first binding domain is sCD4 and the second binding domain is SCFv(17b)." Claims 19, 23-33, 37, 48-49, and 52-54 depend, either directly or indirectly, from claim 1 and thereby incorporate the amendment.

Traunecker *et al.* and Sullivan *et al.* do not teach or suggest all of the elements of the claimed invention. Traunecker *et al.* teaches a fusion protein (wherein the first binding domain is derived from CD4 and the second binding domain is derived from the Fv domain of an anti-CD3 antibody) that is capable of retargeting cytotoxic T lymphocytes (CTLs) onto Human Immunodeficiency Virus (HIV)-infected cells (see abstract, lines 11-12). In addition, Traunecker *et al.* suggests that such proteins can be used to retarget retroviruses to desired cell targets. Thus, Traunecker *et al.* teaches that a fusion protein, specific for **two different cell** surface molecules, can be used i) *to link two different cells*, in order to facilitate the killing of one cell by the other, or ii) *to link a cell to a deficient retrovirus* for somatic gene therapy. Applicants' invention, on the other hand, is a bispecific fusion protein that can bind two different sites on the **same target molecule**. Nothing in Traunecker *et al.* would have taught one of ordinary skill in the art to generate a bispecific fusion protein comprising two domains, both of which bind to the same target molecule.

Sullivan *et al.* teaches the induction of a 17b epitope by sCD4, as well as the virus-neutralizing abilities of the 17b and CG10 antibodies. Sullivan *et al.* does not disclose any type of bispecific fusion proteins, and particularly not one that binds two different sites on gp120, or any other target protein. Thus, Sullivan *et al.* does not overcome the deficiency of Traunecker *et al.* and the combination of these references does not provide all of the limitations of the pending claims. Nor is there any indication in either reference that its teaching can or should be combined with the other.

In light of these arguments and the amendments submitted herein, Applicants respectfully request that this rejection be withdrawn.

Traunecker et al. *in view of Thali* et al.

Claims 1, 11-12, 14-19, 23-34, 37, 48-49, and 52-55 are rejected as allegedly rendered obvious by Traunecker *et al.* in light of Thali *et al.* (*Journal of Virology*, 67(7):3978-3988, 1993). Applicants traverse this rejection.

Claims 11, 12, 14-18 and 55 have been canceled, rendering the rejection of these claims moot. As described above, Applicants have amended claim 1 to recite that the "first binding domain is sCD4 and the second binding domain is SCRv(17b)." Claims 19, 23-32, 48-49, and 52-54 depend, either directly or indirectly, from claim 1 and thereby incorporate the amendment.

Traunecker *et al.* and Thali *et al.* do not teach or suggest all of the elements of the claimed invention. As described above, Traunecker *et al.* teaches that a fusion molecule, specific for **two different cell** surface molecules, can be used i) *to link two different cells*, in order to facilitate the killing of one cell by the other, or ii) *to link a cell to a deficient retrovirus* for somatic gene therapy. Applicants' invention, on the other hand, is a bispecific fusion protein that can bind two different sites on the **same target molecule**. Nothing in Traunecker *et al.* would have taught one of ordinary skill in the art to generate a bispecific fusion protein comprising two domains, both of which bind to the same target molecule.

Thali *et al.* teaches that the 17b and 48d antibodies bind gp120 and neutralize a variety of HIV-isolates. In addition, Thali *et al.* discloses that recognition of the 17b and 48d epitopes by these antibodies is dependent upon the conformation of gp120. However, Thali *et al.* does not disclose any type of bispecific fusion proteins, and particularly not one that binds two different sites on gp120, or any other target molecule. Thus, Thali *et al.* does not overcome the deficiency of Traunecker *et al.* and the combination of these references does not provide all of the limitations of the pending claims. Nor is there any indication in either reference that its teaching can or should be combined with the other.

In light of these arguments and the amendments submitted herein, Applicants respectfully request that this rejection be withdrawn.

CONCLUSIONS

Based on the foregoing amendments and arguments, the claims are in condition for allowance and notification to this effect is requested. If for any reason the Examiner believes that a telephone conference would expedite allowance of these claims, please telephone the undersigned at (503) 226-7391.

Respectfully submitted,

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